## REMARKS

The Office Action dated April 17, 2002 presents the examination of claims 2-10, 12 and 13. Claims 3, 7-8, and 13 are amended. Claims 2, 6, 9, 10, and 12 are canceled. Claims 14 and 15 are added. Upon entry of this Reply, claims 3-5, 7-8 and 13-15 are pending in the application. No new matter is inserted into the application.

***Interview***

Applicant's representative expresses gratitude to the Examiner for the helpful Interview held at the USPTO on July 10, 2002.

***Amendment to the Specification***

During the Interview, the Examiner pointed out that on page 19, lines 14-25, it is disclosed that the excessiveness of the sample DNA is at least B/A, preferably 1.5B/A, and more preferably 2A/B to 1000A/B, and questioned why the fraction changed from B/A to A/B. The reversal of the denominator and numerator is an error. Applicant amends the paragraph herein to correctly recite, "the excessiveness of the sample DNA is at least B/A, preferably 1.5B/A, and more preferably 2B/A to 1000B/A." This correction is obvious

to one of ordinary skill in the art and is therefore not new matter.

***Claim Objections***

The Examiner objects to claims 6 and 7 for allegedly failing to further limit the subject matter of the claims on which they depend. Claim 6 is canceled, thus rendering the objection thereto moot. Applicant respectfully traverses the rejection applied to claim 7. Reconsideration of the claim and withdrawal of the instant objection are respectfully requested.

Claim 7 is directed to the nucleic acid assay process according to claim 13, wherein the labeled standard DNA is prepared by amplification using a primer having introduced therein a region capable of binding to a solid support. Applicant respectfully submits that claim 7 properly limits the subject matter of claim 13, because claim 13 recites that the labeled standard DNA comprises a double stranded nucleic acid having a site capable of binding to a solid support and a detectable label, but claim 13 does *not* specify that the labeled standard DNA is prepared by amplification using a primer having introduced therein a region capable of binding to a solid support.

For the above reasons, Applicant respectfully submits that claim 7 properly limits the subject matter of claim 13, from which it depends. The instant objection is improper and should be withdrawn.

***Rejection under 35 U.S.C. § 112, first paragraph***

*Claims 9-10*

The Examiner rejects claims 9 and 10 under 35 U.S.C. § 112, first paragraph, for allegedly not being described in the specification. Claims 9 and 10 are canceled, thus rendering the rejection moot.

*Claims 2-10, 12, and 13*

The Examiner maintains his rejection of claims 2-10, 12, and 13 under 35 U.S.C. § 112, first paragraph for allegedly not being enabled by the specification. Claims 6, 9, and 10 are canceled, thus rendering rejection thereof moot. Applicant respectfully traverses the rejection applied to the pending claims. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

The Examiner agreed during the interview that very small amounts of target DNA could be detected via the instant method,

even when present in small amounts compared to the wild-type DNA. However, the Examiner argued that the phrase "detection limit" in claim 13 had no clear meaning. In response to the Examiner's remarks, Applicant amends claim 13 to recite that the detection limit is at least $3.6 \times 10^{-6}$ $\mu$g. As presented in the Reply filed on February 6, 2002, this figure represents the weight in one molecule of the mammalian genome. One of ordinary skill in the art would easily calculate this figure as the weight of one molecule of the mammalian genome, and thusly it does not represent new matter.

Alternatively, Applicant also presents claim 14, wherein the phrase "detection limit" is replaced with "theoretical value in $\mu$g," and the amount in $\mu$g of said mutated or polymorphic target DNA is expressed as A and the total amount in $\mu$g of said sample DNA is expressed as B, such that A/B is the fractional equivalent of the percentage of said mutated or polymorphic target DNA in the sample DNA. Support for selecting a theoretical value for said mutated or polymorphic target DNA is found, for example, on page 11, lines 21-23, and page 12, lines 13-18 of the specification. Further, claim 14 also recites that the excessiveness of said sample DNA added to said labeled standard DNA in the competitive hybridization is calculated as the value of B/A.

Finally, Applicant also presents claim 15, directed to the same subject matter as claim 14, but presented in a more concise fashion, for the Examiner's consideration.

Applicant respectfully submits that the amendments to claim 13 fully clarify the meaning therein such that the rejection is overcome and should be withdrawn.

***Rejection under 35 U.S.C. § 112, second paragraph***

The Examiner rejects claims 2-8, 12 and 13 for allegedly being indefinite. Claims 2, 6, and 12 are canceled, thus rendering rejection thereof moot. Applicant respectfully traverses the rejection applied to the pending claims. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

*Claims 12 and 13*

The Examiner points out that claims 12 and 13 recite "the target DNA" in line 17 of claim 12 and line 13 in claim 13, which phrase does not have antecedent basis. In response to the Examiner's remarks, Applicant amends the recitation of "the target DNA" to "said mutated or polymorphic target DNA" in the claims in

pending claim 13. Thus, the instant rejection is overcome.

Similarly, although not pointed out by the Examiner, Applicant noticed that some parts of the claims recite "double stranded sample DNA" while other parts of the claims only recite "sample DNA." In order to maintain consistency throughout all claims, Applicant amends all recitations of "sample DNA" to "double stranded sample DNA" in the claims.

*Claim 13*

The Examiner asserts that the relationship between the "analyte nucleic acid" and the "polymorphic target DNA" is confusing. Applicant clarifies that the analyte nucleic acid is present in a specimen and is amplified into the sample DNA, which contains both wild-type and mutated/polymorphic target DNA. In other words, amplification of the analyte nucleic acid produces the wild-type and/or mutated/polymorphic target DNA.

During the interview, Examiner stated that the expression "wherein said sample DNA comprises both wild-type and mutated or polymorphic DNA in an amplifiable amount" in the third clause of claim 13 was confusing. In response to the Examiner's remarks, Applicant amends the ordering of the expression to "wherein said

sample DNA comprises both mutated or polymorphic DNA and wild type DNA in an amplifiable amount", since this idiomatic amendment results in no change in claim scope.

*Claim 8*

The Examiner asserts that the phrase "is the one prepared by chemical synthesis" does not have sufficient antecedent basis. In response to the Examiner's remarks, Applicant amends claim 8 to delete the words "the one", since this phrase is not necessary. Applicant also found similar wording in claims 6 and 7, although not pointed out by the Examiner, and has amended claims 6 and 7 in a similar manner as claim 8. Thus, the instant rejection is overcome.

Applicant respectfully submits that the instant claims fully comply with 35 U.S.C. § 112, second paragraph. Withdrawal of the instant rejection is respectfully requested.

***Summary***

Applicant respectfully submits that the above amendments and remarks alleviate the Examiner's outstanding rejections such that

the present invention is in a condition for allowance. Favorable action and early allowance of the claims are respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Kristi L. Rupert, Ph.D. (Reg. No. 45,702) at 703/205-8000 in the Washington Metropolitan Area.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachment: Version with Markings to Show Changes Made

(Rev. 02/12/01)

VERSION WITH MARKINGS TO SHOW CHANGES MADE

*In the Specification*:

The paragraph on page 19, lines 14-25, is amended as follows:

The procedure of excessiveness determination is not particularly limited, and the excessiveness may be typically determined such that, when the detection limit selected for the target DNA which is the same as the labeled standard DNA and which is present in the sample DNA is A/B, the excessiveness of the sample DNA may be at least B/A, preferably 1.5B/A, and more preferably [2A/B to 1000A/B] 2B/A to 1000B/A. The sample DNA may be preliminarily quantitated for the amount of DNA (total content) in the sample DNA by such means as electrophoresis, UV irradiation or absorption so that an adequate amount of DNA may be added in accordance with the excessiveness.

*In the Claims*:

Claims 2, 6, 9, 10, and 12 are canceled.

The following claims are amended:

3. (Four Times Amended) A nucleic acid assay process according to claim 13, wherein [the] said mutated or polymorphic

target DNA which is the same as said labeled standard DNA and which is present in said sample DNA is quantitated by evaluating the degree of exchange of the complementary strands between said sample DNA and said labeled standard DNA at the selected excessiveness of said sample DNA, wherein said exchange occurs at a higher frequency when [the] said mutated or polymorphic target DNA is the same as the labeled standard DNA, and said label intensity is reduced.

7. (Three Times Amended) A nucleic acid assay process according to claim 13, wherein the labeled standard DNA is [the one] prepared by [gene] amplification using a primer having introduced therein a region capable of binding to a solid support.

8. (Three Times Amended) A nucleic acid assay process according to claim 13, wherein the labeled standard DNA is [the one] prepared by chemical synthesis.

13. (Four Times Amended) A nucleic acid assay process for identifying and/or quantifying a mutation or polymorphism in a double stranded sample DNA prepared by amplification of a particular region of an analyte nucleic acid which is present in a

specimen, comprising the steps of:

providing labeled standard DNA having a nucleotide sequence the same as a mutated or polymorphic target DNA of interest, wherein said labeled standard DNA comprises a double stranded nucleic acid having a site capable of binding to a solid support on one strand and a detectable label on the other strand;

amplifying said particular region of said analyte nucleic acid which is present in said specimen to prepare said double stranded sample DNA[,] for competitive hybridization, wherein said sample DNA comprises both [wild-type and] mutated or polymorphic target DNA and wild-type DNA in an amplifiable amount;

selecting a detection limit for said mutated or polymorphic target DNA, wherein when the detection limit for the target DNA present in said sample DNA is A/B, the excessiveness of said sample DNA is at least B/A, and wherein A/B is the fractional equivalent of the percentage of said mutated or polymorphic target DNA content in the sample DNA and A is at least $3.6 \times 10^{-6}$ $\mu g$;

adding an excessive amount in $\mu g$ of said sample DNA to said labeled standard DNA, to allow competitive hybridization to take place between said mutated or polymorphic target DNA and labeled standard DNA under conditions which allow for hybridization of at

least some of said labeled standard DNA and under conditions wherein non-target sample DNA does not hybridize with said labeled standard DNA, wherein the excessiveness of said sample DNA added to said labeled standard DNA in the competitive hybridization is calculated as the value of B/A [selected in accordance with the pre-selected detection limit],

detecting the hybridized labeled standard DNA by utilizing said detectable label and said site capable of binding to a solid support; and

evaluating the degree of exchange that occurred during competitive hybridization of the complementary strands between said sample DNA and said labeled standard DNA.

Claims 14 and 15 are added.